REMARKS

This amendment is in response to the Final Office Action, dated August 11, 2005 ("Final Office Action"). It is respectfully submitted that the application is in condition for allowance. Claims 1, 3-8, 10-18, 20 and 22-24 were pending and rejected; claims 2, 9, 19 and 21 having previously been canceled. Claims 6, 14, 16 and 22 have been amended. Claims 25-28 have been added. Following entry of the present amendment claims 1, 3-8, 10-18, 20 and 22-28 are pending. No new matter has been added. Allowance and reconsideration of the application in view of Applicants' amendment and the ensuing remarks is respectfully requested.

Claim 6 has been amended to correct the misspelling of "particles".

Claim 14 has been amended to more particularly describe that which Applicants regard as their invention. Claim 14 as amended, describes a method "of producing a cell matrix" which includes suspending cells in a medium that includes a tissue powder derived from a biological material. Support for this amendment may be found throughout the Specification; for instance on page 4, lines 13-28.

Claim 16 and 22 have also been amended to more particularly describe that which Applicants regard as their invention. Claim 16, as amended, describes the cells "that are provided and suspended" of claim 14 are the same as "a type of cells present in" the biological material. Claim 22, as amended, describes the cells "that are provided and suspended" of Claim 14 are different from "a type of cells present in" the biological material. Support for this amendment may be found throughout the Specification; for instance, at page 5, lines 7-13.

New claims 25 and 26 have been added, and describe a "cell culture matrix composition" derived from a tissue powder derived from "a full and intact whole organ". New claim 26 further includes "a medium". Support for these new claims may be found throughout the Specification; for instance at page 4, lines 8-9, page 5, lines 1-3, and page 7, lines 1-24.

New claim 27 has been added, and describes "a cell culture matrix composition" including a "fine tissue powder" derived from a "full and intact whole organ". Further, the "fine tissue powder" is produced by grinding and sonicating procedures. Support for

this new claim may be found throughout the Specification; for instance, at page 5, lines 24-28.

New claim 28 has been added, and describes "a method of producing a cell matrix by providing cells" and "suspending the cells in a medium" with a tissue powder derived from a "full and intact whole organ". Support for this new claim may be found throughout the Specification; for instance at page 4, lines 8-9, page 5, lines 1-3, and 24-28, and page 7, lines 1-24.

Examiner objected to Claim 6 due to the misspelling of "particles". Claim 6 has been amended to correct the spelling of "particles". Applicants therefore respectfully request withdrawal of this objection.

Examiner rejected claims 14-18, 20 and 22 under 35 U.S.C. §112, second paragraph. Specifically, Examiner found these claims to be vague and indefinite, their metes and bounds unclear. Examiner suggested inserting "of producing a cell matrix" after "method" and deleting the ",". Furthermore, Examiner found that 16 and 22 are unclear for the recitation of "at least partially" because it is "unclear which part would not constitute the biological material." These rejections under 35 U.S.C. §112, second paragraph are respectfully traversed.

First, Applicants have adopted Examiner's suggestions of inserting "of producing a cell matrix" after "method" and deleting the ",".

Second, Applicants respectfully submit that Claims 16 and 22, as amended are not unclear. Cells exhibit optimal growth and differentiation when cultured in a matrix derived from the same organ with which the cells being cultured are associated (*see* Specification, page 5, lines 7-13). For example, it is believed that hepatocytes will exhibit optimal growth and differentiation when cultured in a matrix derived from a full and intact whole liver or a portion (e.g., a slice) of a full and intact whole liver.

As claimed in amended Claim 16, the cells that are provided and suspended are the same type as a type of cells present in the biological material from which the tissue powder was derived. For example, in a liver, hepatocytes and other types of liver cells would be present; however neural cells would typically not be present. The cells that

are provided and suspended in a matrix derived from a liver may be hepatocytes, but may not be neural cells, as neural cells are not typically present in the liver.

As claimed in amended Claim 22, the cells that are provided and suspended are a different type compared to the cells that would be present in the biological material from which the tissue powder was derived. Again, for example in a liver, hepatocytes and other types of liver cells would be present; however neural cells would typically not be present. The cells that are provided and suspended in a matrix derived from a liver, in Claim 22, may be neural cells, even though neural cells are not typically found in the liver.

Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 25 U.S.C. §112, second paragraph.

Examiner rejected Claims 1 and 3 under 35 U.S.C. §102(b) as being anticipated by Badylak *et al.* (U.S. Patent No. 5,515,533) (hereinafter "Badylak I"). Examiner found that Badylak I teaches "a cell culture matrix composition comprising a tissue powder derived from an intestinal segment and the composition may further comprise a medium." Additionally, Examiner stated that the abstract in Badylak I teaches a "cell culture matrix derived from the intestinal submucosa comprising a segment of intestinal tissue." Furthermore, Examiner stated that Badylak I teaches that the intestine segment used to prepare the disclosed cell matrix composition does not have to be digested and is comminuted; and that Applicants' definition of the term "whole" denotes that the biological materials are not decellularized or digested. Still further, Examiner stated that "the open ended term 'comprising' does not necessarily omit a tissue powder derived from intestinal segment as disclosed by Badylak [I]". This rejection is respectfully traversed.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference (MPEP §2131 (citing Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987))). Furthermore, an Applicant may be his or her own lexicographer as he is "permitted to use his or her own terminology" (*see* MPEP §608.01(g)).

Badylak I does not describe the cell culture matrix composition of the present invention as set forth in Applicants' independent claim 1, as previously amended and from which claim 3 depends.

First, the abstract of Badylak I does not teach a "cell culture matrix derived from the intestinal submucosa comprising a segment of intestinal tissue," as asserted by Examiner. Quite to the contrary, the abstract states that the tissue graft material is "prepared from the intestinal submucosa comprising the tunica submucosa, the muscularis mucosa and the stratum compactum **of a segment** of intestinal tissue..." (emphasis added.) (*See also* Badylak I Col. 2, lines 30-35.) This clearly conveys that the entire segment of the intestinal tissue is not used.

Second, the aforementioned layers are "delaminated from the tunica muscularis and the luminal portion of the tunica mucosa of said segment" (Col. 2, lines 30-35). Again, these layers are merely a few of the many layers that comprise a "segment" of the small intestine. This is plainly described in U.S. Patent No. 4,902,508, which is specifically incorporated by reference in Badylak I for the purpose of describing the process of obtaining only certain layers from a segment of small intestine (Col. 3, lines 26-31 and 53-61, and Fig. 1 of the '508 patent). Specifically, as described in Badylak I and the '508 patent to which it refers, a segment of intestine includes seven layers (illustrated as A-G in Fig. 1 of the '508 patent); however, the compositions of Badylak I include only three of these seven layers.

In contrast to Badylak, the compositions of Applicants' invention, as claimed, are based on a tissue powder derived from a full and intact whole organ, tissue or portion thereof. The purpose of having the full and intact whole organ, tissue or portion thereof (*e.g.*, a cross-sectional segment or a slice of the full and intact whole organ or tissue) is that it provides a more comprehensive biological support for cell culture (*see* Specification at p. 5, lines 26-28). As such, Applicants' use of "portion" has a specific connotation. Applicants are allowed to impart a specific definition to the term "portion" and Applicants have given the term "portion" a specific connotation. By "portion", it is meant that the portion of the full and intact whole organ or tissue will generally have the same composition as the full and intact whole organ or tissue; for example, a cross-sectional segment of a small intestine or a slice of a liver. The physiologically distinct

layers of intestinal submucosa described in Badylak I are clearly neither a full and intact whole organ nor a full and intact whole tissue. Furthermore, the selected layers of the submucosa of Badylak I are not a "portion" of a full and intact whole organ or tissue, as that term is used in Applicants' invention. Badylak I specifically indicates that it is based on three of seven layers of a "segment of small intestine," while Applicants' claims will require the entire segment (*i.e.*, a cross-sectional segment which generally has the same composition as the full and intact whole small intestine).

Furthermore, Applicants' use of "portion" excludes tissue powder as disclosed by Badylak I because Badylak I uses a few layers of a segment of an intestine rather than using the entire cross-sectional segment of the intestine. Applicants' use of the open term "comprising" is irrelevant, because Applicants' claim does necessarily omit a composition that merely contains a tissue powder as disclosed by Badylak I. If an entire segment (i.e., a cross-sectional segment) of the intestine is not used in preparing a tissue powder, the powder will not fall within the scope of the claims.

Accordingly, Badylak I does not anticipate Applicants' independent claim 1, and claim 3 that depends therefrom, as it does not describe the inventive tissue powder.

In light of the foregoing remarks, Applicants respectfully submit that Badylak I does not anticipate claims 1 or 3, and therefore request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b).

Examiner rejected Claims 4-5, 11 and 13 under 35 U.S.C. §102(b) as being anticipated by Badylak I. Specifically, Examiner found that Badylak I "teaches that the intestine segment used to prepare the disclosed cell matrix composition does not have to be digested and is comminuted..." Additionally, Examiner stated that "the open ended term "comprising" does not necessarily omit a tissue powder derived from intestinal segment as disclosed by Badylak [I]". Furthermore, Examiner stated that Applicants claimed that the critical feature of the invention is the "whole segment" and that this feature is anticipated by Badylak I's teachings of its cell culture matrix derived from the intestinal submucosa comprising a segment of intestinal tissue. Still further, Examiner stated that the term "whole" as used by Applicants does not imply that a full

and intact organ is necessarily processed, but that the organ, tissue or a portion thereof is processed in undigested form. This rejection is respectfully traversed.

Again, Badylak I does not describe the method for producing tissue powder of the present invention as set forth in independent claim 4, as previously amended and from which the remaining rejected claims depend, for reasons similar to that described above with respect to Applicants' claim 1. In short, the compositions of Applicants' invention, as claimed, are based on a tissue powder derived from a full and intact whole organ, tissue or portion thereof. The purpose of having the full and intact whole organ, tissue or portion thereof (*e.g.*, a cross-sectional segment or a slice of the full and intact whole organ or tissue) is that it provides a more comprehensive biological support for cell culture (*see* Specification at p. 5, lines 26-28). As such, Applicants' use of "portion" has a specific connotation. By "portion", it is meant that the portion of the full and intact whole organ or tissue will generally have the same composition as the full and intact whole organ or tissue; for example, a cross-sectional segment of a small intestine or a slice of a liver. Baydlak I does not describe a full and intact whole organ, tissue or portion thereof (*e.g.*, a cross-sectional segment or a slice of a full and intact whole organ or tissue), as is required by Applicants' independent claim 4. Badylak I specifically indicates that it is based on three of seven layers of a "segment of small intestine," while Applicants' claims require the entire segment (*i.e.*, a cross-sectional segment).

While a feature of Applicants' present invention is the use of biological materials that are not decelluarized or digested to provide a cell support matrix, another important feature is the use of the full and intact whole organ, tissue, or portion thereof. Again, by "portion" it is meant that the portion of the full and intact whole organ or tissue will have the same composition as the full and intact whole organ or tissue; for example, a cross-sectional segment of a full and intact whole small intestine or a slice of a full and intact whole liver.

Again, Applicants' use of "portion" excludes tissue powder as disclosed by Badylak I because Badylak I uses a few layers of a segment of an intestine rather than using the entire cross-sectional segment of the intestine. Applicants' use of the open term "comprising" is irrelevant, because Applicants' claim does necessarily omit a

composition that merely contains a tissue powder as disclosed by Badylak I. If an entire segment (i.e., a cross-sectional segment) of the intestine is not used in preparing a tissue powder, the powder will not fall within the scope of the claims.

Therefore, Badylak I does not anticipate Applicants' independent claim 4, and the remaining rejected claims that depend therefrom.

In light of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §102 (b).

Examiner rejected Claims 1, 3-5, 11, 13-15, 20 and 24 under 35 U.S.C. §102(b) as being anticipated by Badylak et al. (U.S. Patent No 5,866,414) (hereinafter "Badylak II"). Specifically, Examiner stated that Badylak II teaches "cell culture matrix composition comprising a tissue powder, method of producing the tissue powder, and method of producing a cell culture matrix and wherein the matrix composition contains portion of a whole liver and medium."

Applicants strongly disagree with Examiner concerning Badylak II's alleged disclosure of the use of a portion of a whole liver to produce a matrix composition. Badylak II does not teach the use of a portion of a whole liver to produce a matrix composition. Indeed, Applicants respectfully submit that Examiner is mistaken -- there is no disclosure in Badylak II of the use of a liver to produce a matrix composition. Rather, Badylak II first recognizes that hepatocytes are among cell types that are difficult to culture (*see* Badylak II, page 3, col. 2, lines 63-65). Second, the matrix composition disclosed by Badylak II remains derived from submucosal tissue (*see* Badylak II, page 4, col. 3, lines 2-15). Badylak II merely disclosed that it believed that hepatocytes may be cultured using its cell culture composition (derived from intestinal submucosa) (*see* Badylak II, page 5, col. 6, lines 14-29.). Thus, the source of the hepatocytes to the cell culture matrix is the hepatocytes to be cultured by the matrix composition. In other words, Badylak II does not use a liver or a portion of a liver to produce the matrix composition. Therefore, at a minimum, Badylak does not teach the use of a liver (full and intact, whole, digested, decellularized, portion or otherwise) to produce a matrix composition.

Furthermore, Applicants' matrix composition is derived from a full and intact whole organ, tissue or a portion thereof, including a full and intact whole liver or a portion thereof (*e.g.*, a slice of the liver). As previously noted, the purpose of having the full and intact whole organ, tissue or portion thereof (*e.g.*, a cross-sectional segment or a slice of the full and intact whole organ or tissue) is that it provides a more comprehensive biological support for cell culture (*see* Specification at p. 5, lines 26-28). Badylak II does not teach any such composition.

Therefore, Badylak II does not anticipate Applicants' independent claims 1, 4, 14, 24, and the remaining rejected claims that depend therefrom.

In light of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §102 (b).

Examiner rejected Claims 1, 3-6, 8, 11, 13, and 23 under 35 U.S.C. §102(a) as being anticipated by Yang, et al. (U.S. Patent Publication No. 2002/0183857; hereinafter "Yang"). Specifically, Examiner stated that Yang teaches a "cell culture matrix composition comprising tissue powder and method for producing the tissue powder." Examiner further stated that Yang teaches "a segment of blood vessel from which a powder is derived as the tissue composition." This rejection is respectfully traversed.

For many of the same reasons noted above with respect to Badylak and the layers of intestinal submucosa, Yang does not anticipate Applicants' invention as claimed. Yang does not utilize an entire segment of the blood vessel (*i.e.*, a cross-sectional segment of a blood vessel). Rather, Yang utilizes several layers of the blood vessels and specifically removes the endothelial layer and part of the aventitia layer from being part of the composition (*see* Yang, page 4, para. 33).

Again, Applicants' inventive composition utilizes a full and intact whole organ or tissue or a portion thereof. The purpose of having the full and intact whole organ, tissue or portion thereof (*e.g.*, a cross-sectional segment or a slice of the full and intact whole organ or tissue) is that it provides a more comprehensive biological support for cell culture (*see* Specification at p. 5, lines 26-28). "Portion" has a specific connotation in Applicants' invention. It is meant that the portion of the full and intact whole organ or

tissue will have generally the same composition as the full and intact whole organ or tissue; for example, a cross-sectional segment of a blood vessel or a slice of a liver.

The selected layers of blood vessels described in Yang are clearly neither a full and intact whole organ nor a full and intact whole tissue. Furthermore, the selected layers of the blood vessel in Yang are not a "portion" of a full and intact whole organ or tissue, as that term is used in Applicants' invention. Yang specifically indicates the removal of the endothelial layer and part of the aventitia layer from being part of the composition, while Applicants' claims require all the layers of a blood vessel (*i.e.*, a cross-sectional segment of the blood vessel).

Therefore, Yang does not anticipate Applicants' independent claims 1, 4, 23 and the remaining rejected claims that depend therefrom.

In light of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §102 (a).

Examiner rejected Claims 1, 3-8, 10-18, 20 and 22-24 under 35 U.S.C. §103(a) as being unpatentable over Badylak et al. (Examiner did not indicate which Badylak patent is used for the rejection and thus Applicants have responded with the presumption that both patents are relied upon), Weiss, et al., and Vail et al. Specifically, Examiner stated that the intestinal tissue disclosed by Badylak I & II is not less than a "portion." Further, Examiner stated that even using Applicant's definition of "whole", one of skill in the art would have been motivated to use a portion of intestinal tissue as disclosed by Badylak I & II because the references teach that the powder is obtained without digestion of the tissue. Furthermore, Examiner stated that sonication and perfusion are clearly disclosed by the cited prior art secondary references and one of skill would have been motivated to use these techniques because they are disclosed to be useful for the preparation of similar products as claimed by Applicants. This rejection is respectfully traversed.

Three basic criteria must be met to establish a prima facie case of obviousness: (1) "*there must be some suggestion or motivation . . . to combine reference teachings*," (2) "*there must be a reasonable expectation of success*," and (3) the prior art references "*must teach or suggest all the claim limitations*." MPEP § 2142 (emphasis added).

For the reasons set forth above, Badylak does not teach or suggest all of the claim limitations, as amended. The reference does not describe the inventive compositions or methods. The reference teaches the use of layers of an intestine that are less than a "portion" of a full and intact whole organ as described in Applicants' claims. In accordance with Applicant's claims, if a portion of an organ or tissue is used, the portion will generally have the same composition as the full and intact whole organ or tissue. In contrast, if merely layers of a segment of the small intestine are used as disclosed by Badylak I & II, it will not fall within the scope of Applicants' claims. Applicants agree with Examiner that, in addition to these shortcomings, Badylak does not describe the use of perfusion or sonication techniques. However, while Applicants in no way concede that Examiner's combination of references is proper herein, even if the combination is proper, the cited combination of references -- supplementing the aforementioned references with information regarding perfusion and sonication techniques -- still does not teach or suggest all of the limitations of Applicants' claims.

In light of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

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All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. If for any reason Examiner finds the application other than in condition for allowance, Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (213) 633-6800 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,
Yutaka Umehara *et al.*
DAVIS WRIGHT TREMAINE LLP

By _____
Seth D. Levy, Esq.
Registration No. 44,869

Enclosures:
Postcard

Petition for one-month extension of time
Request for Continued Examination

865 South Figueroa Street, Suite 2400
Los Angeles, CA 90017-2566
Phone: (213) 633-6800
Facsimile: (213) 633-6899